

**Practitioner's Docket No. MPI97-057P1RCP1CN1M**

**IN THE CLAIMS:**

Kindly cancel claims 3, 6, 10-13, 15-22, 24, 28-29, 32, 35, 39-42, 45, 48, 52-55, 57-58; and amend claims 4, 5, 7, 8, 9, 23, 25, 26, 27, 33, 34, 36, 38, 46, 47, 49, 50, 51, and 56.

This listing of claims will replace all prior versions, and listings, of claims in the application:

**STATUS OF THE CLAIMS:**

1. Purified NEDD8-activating protein beta subunit.
2. The purified NEDD8-activating protein beta subunit according to claim 1 having the amino acid sequence shown in Figure 1.
3. cancelled
4. (herein amended) The NAE1-beta expression element selected from isolated or recombinant nucleic acid sequences encoding NAE1-beta according to claim 1 or nucleic acid sequences specifically homologous or specifically complementary thereto, vectors comprising any such nucleic acid sequences, and recombinant expression units which express NAE1-beta, antisense transcripts, or dominant negative mutants thereof.
5. (herein amended) A method for identifying NAE1BBMs comprising contacting purified NAE1-beta according to ~~the invention~~ claim 1 and populations of molecules or mixed populations of molecules and determining the presence of molecules which bind specifically to NAE1-beta.
6. cancelled
7. (herein amended) A method for determining the presence or absence and/or quantity of NAE1-beta, NAE1 heterodimer, or NAE1 heterodimer/NEDD8 complex comprising NAE-1 beta according to claim 1, in a biological sample, the method comprising providing a detectable NAE1BBM to a biological sample, allowing the detectable NAE1BBM to bind to NAE1-beta, NAE1 heterodimer, or NAE1 heterodimer/NEDD8 complex, if any is present in the biological sample, and detecting the presence or absence and/or quantity of a complex of the detectable NAE1BBM and NAE1-heterodimer, or NAE1 heterodimer/NEDD8 complex.

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8. (herein amended) A method for determining the presence or absence and/or quantity of NAE1-beta nucleic acid according to claim 1 in a biological sample comprising providing to the biological sample a nucleic acid sequence which is specifically complementary to NAE1-beta nucleic acid.
9. (herein amended) A method for identifying modulating ligands of NAE1-beta comprising providing NAE1BBMs to an assay system for NAE1-beta participation in the NEDD8-activation/conjugation pathway comprising NAE1-beta according to claim 1, and determining whether such NAE1BBMs interfere with or enhance the ability of NAE1-beta to participate in the NEDD8-activation/conjugation pathway.
- 10-13 (cancelled)
14. A method for identifying NAE1ABMs comprising screening for NAE1ABMs by contacting purified NAE1-alpha and populations of molecules or mixed populations of molecules and determining the presence of molecules which bind specifically to NAE1-alpha.
- 15-22 cancelled.
23. (herein amended) A method for modulating the activation and/or conjugation of NEDD8 comprising providing a modulating ligand of NAE1-beta or NAE1-alpha or a recombinant expression unit which expresses NAE1-beta according to claim 1 or NAE1-alpha or an antagonist thereof to a biological system in which NEDD8 is conjugated to another protein.
24. cancelled
25. (herein amended) A method for modulating APP function and/or beta peptide accumulation in a biological system comprising providing a modulating ligand of NAE1-beta or NAE1-alpha or a recombinant expression unit which expresses NAE1-beta according to claim 1 or NAE1-alpha or an antagonist thereof to a biological system.
26. (herein amended) A purified complex of NAE1-beta according to claim 1 and NAE1-alpha, or a purified complex of portions thereof.
27. (herein amended) A The purified complex of NAE1-beta, NAE1-alpha of claim 26, further comprising and NEDD8, or a purified complex of portions thereof.

28.-29 cancelled

30. Purified NEDD8-conjugating enzyme 1.

31. The purified NEDD8-conjugating enzyme 1 according to claim 30 having the amino acid sequence shown in Figure 1.

32. cancelled

33. (herein amended) ~~The~~ An NCE1 expression element capable of expressing a NEDD8-conjugating enzyme according to claim ~~32~~ 30 selected from isolated or recombinant nucleic acid sequences encoding NCE1 or dominant negative mutants thereof, or expressing antisense transcripts thereof or nucleic acid sequences specifically homologous or specifically complementary thereto, vectors comprising any such NCE1 expression elements.

34. (herein amended) A method for identifying NCE1BMs comprising contacting purified NCE1 according to claim 30 and populations of molecules or mixed populations of molecules and determining the presence of molecules which bind specifically to NCE1.

35. cancelled

36. (herein amended) A method for determining the presence or absence and/or quantity of NCE1 or NCE1/NEDD8 complex in a biological sample, the method comprising providing a detectable NCE1BM to a biological sample, allowing the detectable NCE1BM to bind to NCE1 according to claim 30, or NCE1/NEDD8 complex, if any is present in the biological sample, and detecting the presence or absence and/or quantity of a complex of the detectable NCE1BM and NCE1 or NCE1/NEDD8 complex.

37. A method for determining the presence or absence and/or quantity of NCE1 nucleic acid in a biological sample comprising providing to the biological sample a nucleic acid sequence which is specifically complementary to NCE1 nucleic acid.

38. (herein amended) A method for identifying modulating ligands of NCE1 comprising providing NCE1BMs to an assay system for NCE1 participation in the NEDD8-activation/conjugation pathway, comprising NCE according to claim 30, and determining whether such NCE1BMs interfere with or enhance the ability of NCE1 to participate in the NEDD8-activation/conjugation pathway.

39-42 cancelled

43. Purified NEDD8-conjugating enzyme 2.

44. The purified NEDD8-conjugating enzyme 2 according to claim 43 having the amino acid sequence shown in Figure 4.

45. cancelled

46. (herein amended) ~~The~~ An NCE2 expression element capable of expressing NEDD8-conjugating enzyme 2 according to claim 45 ~~43~~ selected from isolated or recombinant nucleic acid sequences encoding NCE2 or dominant negative mutants thereof, or expressing antisense transcripts thereof or nucleic acid sequences specifically homologous or specifically complementary thereto, and vectors comprising any such NCE2 expression units.

47. (herein amended) A method for identifying NCE2BMs comprising contacting purified NCE2 according to claim 43 and populations of molecules or mixed populations of molecules and determining the presence of molecules which bind specifically to NCE2.

48. cancelled

49. (herein amended) A method for determining the presence or absence and/or quantity of NCE2 or NCE2/NEDD8 complex in a biological sample, the method comprising providing a detectable NCE2BM to a biological sample, allowing the detectable NCE2BM to bind to NCE2 according to claim 43, or NCE2/NEDD8 complex, if any is present in the biological sample, and detecting the presence or absence and/or quantity of a complex of the detectable NCE2BM and NCE2 or NCE2/NEDD8 complex.

50. (herein amended) A method for determining the presence or absence and/or quantity of NCE2 nucleic acid in a biological sample comprising providing to the biological sample a nucleic acid sequence which is specifically complementary to NCE2 nucleic acid encoding NCE2 according to claim 43.

51. (herein amended) A method for identifying modulating ligands of NCE2 comprising providing NCE2BMs to an assay system for NCE2 participation in the NEDD8-activation/conjugation pathway, comprising NCE2 according to claim 43, and determining whether such NCE2BMs interfere with or enhance the ability of NCE2 to participate in the NEDD8-activation/conjugation pathway.

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52-55 cancelled

56.(herein amended) A purified complex of NCE1 according to claim 30 and NEDD8, or a purified complex of portions thereof.

57. cancelled

58. cancelled.